Office Action Summary	Application No. 10/568,409	Applicant(s) LALEV ET AL.
	Examiner Leon Y. Lum	Art Unit 1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 05 November 2010.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-26,29-32 and 34-52 is/are pending in the application.

4a) Of the above claim(s) 29-31,36,41-44 and 47-52 is/are withdrawn from consideration.

5)☒ Claim(s) 1-26,32,34,35,37-40,45 and 46 is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 10/7/2010 .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 29-31, 36 and 47-49 are objected to because of the following informalities: the claims have an incorrect status identifier. Since the claims are withdrawn as being directed to non-elected species, they should be identified as "Withdrawn." Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5-6, 8-9, 22-23, 32, 34-35 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Publication No. 2004/0142488 to Gierde *et al.* ("Gierde") in view of U.S. Patent No. 7,379,820 to Sukits *et al.* ("Sukits").

i. Independent claims 1 and 2 are obvious

Gierde describes a method for performing affinity chromatography, in which an affinity molecule fixed on a column captures a biomolecule. *See* paragraphs 0083-0092. The biomolecule can be a multi-protein complex. *See* paragraphs 0195-0201; Table 1. With this description, Gierde teaches steps (a)-(b) of claim 1 and steps (c)-(d) of claim 2. One constituent of the multi-protein complex can be recovered while the rest of the complex remains immobilized on the affinity column. *See* paragraph 0200. Notably, this section of Gierde is supported by priority document U.S. Patent App. 60/396,595, which describes an antibody-antigen complex that is bound to an affinity column through biotin-streptavidin bonds and wherein the antigen, but not the antibody, is eluted. *See* page 95 of the 199 page document. Gierde also teaches step (c) of claim 1 and step (e) of claim 2 by describing a wash step. *See* paragraph 0137.

Regarding claim 2, Gierde teaches a protein fusion tag for purifying recombinant proteins. *See* paragraph 0090. This description is also supported by the '595 priority document. *See* page 32 of the 199 page document. Accordingly, Gierde necessarily teaches steps (a)-(b).

Gierde does not, however, teach first and second ligands that associate through electrostatic forces or step (d) of claim 1 or step (f) of claim 2 – i.e., recovering one of the constituents through decreasing the electrostatic force between it and the rest of the multi-protein complex.

Sukits describes a series of protein pairs – e.g., TRADD and RIP and TNFR-1 and TRADD – that associate together *in vivo* through electrostatic interaction, *see* column 1, lines 21-38, but can be separated by using NaCl to disrupt the electrostatic interaction. *See* column 18, lines 30-38. The interaction of these proteins *in vivo* leads to the activation of transcription factor NFκB. *See* column 1, lines 21-24.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Gierde's method to isolate a protein from a protein pair by using NaCl to disrupt electrostatic interaction, as taught by Sukits. By combining Gierde and Sukits, Gierde's method would be modified to include a NaCl elution step on one of the immobilized protein-protein complexes described by Sukits. In this manner, the NaCl elution would separate one protein within the complex from other proteins. The skilled artisan would have made the modification because Sukit's technique allows the skilled artisan to purify and concentrate one of the proteins involved in NFκB activation to analyze this signaling pathway in an individual. Indeed, since Gierde indicates that

analytes can be purified using affinity chromatography for various purposes, *see* paragraphs 0225-0226, including analyzing protein-protein interactions, the skilled artisan would recognize that analyzing a signaling pathway by isolating one of its constituents falls within Gierde's purpose. Moreover, since Gierde does not limit the elution to any particular method, the skilled artisan would have had a reasonable expectation of success in combining Sukits's technique with Gierde's affinity chromatography method.

ii. Dependent claims 5-6, 8-9, 22-23, 25-26, 32, 34-35 and 38-40 are obvious

Regarding claim 5, Gierde teaches an antibody affinity molecule that binds to a protein antigen within a multi-protein complex. *See* Table 1.

Regarding claim 6, Gierde teaches the Fc region of Protein A. *See* paragraph 0091.

Regarding claims 8 and 9, Gierde teaches GST and MBP tags. *See* paragraph 0092.

With respect to claims 22 and 23, the NaCl gradient incorporates an increasing ionic strength gradient, especially since the objective is to separate one protein from the other. *See supra* rejection of claim 1.

Regarding claims 25 and 26, since Sukits describes a NaCl elution medium, it would have been obvious to one of ordinary skill in the art to select a change in concentration using the ranges claimed. Indeed, the skilled artisan would have arrived at the claimed ranges based on the doctrine of routine optimization. In a case decided by the precursor to the Federal Circuit, the court stated that a claim is not allowable

where the skilled artisan could have arrived at the claim through routine experimentation on the optimum or workable ranges of the claim. *In re Aller*, 220 F.2d 454, 456 (CCPA 1955) (stating "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."). Here, Gierde and Sukits teach all the limitations of claims 25 and 26, except for a concentration range. It would have been within the routine skill of the skilled artisan to optimize the concentration ranges of the NaCl elution compound to arrive at the claimed ranges.

Regarding claim 32, Gierde describes the step of repeating the assay with cell lysates. *See* paragraphs 0138 and 0155.

Regarding claim 34, NaCl is capable of separating one protein from the other, thereby having “capability” to separate the “first ligand from the second ligand,” as claimed.

With respect to claim 35, Sukits describes a mutation. *See* column 18, lines 43-45. As held by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 USPQ2d 1385 (U.S. 2007), an obvious to try rationale is proper, given a "finite number of identified, predictable solutions.” *KSR* at 1397. Indeed, the Court stated that in such a case, “a personal of ordinary skill has good reason to pursue the known options within his or her technical grasp." *Id*. Here, as would have been recognized by one of ordinary skill in the art, it would have been obvious to try a mutated FADD protein in order to analyze the interaction of the protein with FAS.

With respect to claim 38, one of ordinary skill in the art would have found it obvious to include an electrostatic charge identical to a mutation (species (b) in the claim) since the object of the combination of Gierde and Sukits is to separate the protein constituents. Moreover, since Gierde teaches a gradient, *see* paragraph 0180, the skilled artisan would have found it obvious to include the claimed electrostatic charge in the range of NaCl concentrations.

Regarding claims 39-40, Gierde describes enzyme and polypeptide interactions. See paragraph 0091.

Claims 3-4 and 10-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Publication No. 2004/0142488 to Gierde *et al.* ("Gierde") in view of U.S. Patent No. 7,379,820 to Sukits *et al.* ("Sukits").

i. Independent claims 3 and 4 are obvious

Gierde describes a method for performing affinity chromatography, in which an affinity molecule fixed on a column captures a biomolecule. *See* paragraphs 0083-0092. The biomolecule can be a multi-protein complex. *See* paragraphs 0195-0201; Table 1. One constituent of the multi-protein complex can be recovered while the rest of the complex remains immobilized on the affinity column. *See* paragraph 0200. Notably, this section of Gierde is supported by priority document U.S. Patent App. 60/396,595, which describes an antibody-antigen complex that is bound to an affinity column through biotin-streptavidin bonds and wherein the antigen, but not the antibody, is eluted. *See* page 95 of the 199 page document. Moreover, the multi-protein complex

can be a fusion protein. *See* paragraph 0090. This description is also supported by the '595 priority document. *See* page 32 of the 199 page document. Accordingly, Gierde teaches steps (a)-(d) and (i), except for two affinity tags.

Gierde also teaches step (e) describing a wash step. *See* paragraph 0137.

However, Gierde does not teach first and second ligands that associate through electrostatic forces, step (a) to the extent that it teaches two affinity tags, and steps (f) and (g)-(h).

Sukits describes a series of protein pairs – e.g., TRADD and RIP and TNFR-1 and TRADD – that associate together *in vivo* through electrostatic interaction, *see* column 1, lines 21-38, but can be separated by using NaCl to disrupt the electrostatic interaction. *See* column 18, lines 30-38. The interaction of these proteins *in vivo* leads to the activation of transcription factor NFκB. *See* column 1, lines 21-24.

Rigaut describes a tandem affinity purification method, including performing a two-step affinity purification process in which a TAP-tagged target protein is bound to a first affinity column through a first tag, the target protein is then cleaved from the first tag and bound to a second affinity column through a second tag. *See* page 1030 (entire page). The target protein prior to the affinity separation steps can be bound to another protein (corresponding to the claimed "first ligand"). *Id.* (Figure 1, depicting the target protein attached to "associated proteins"). The TAP-tagged protein and other protein come into contact *in vivo*, prior to the extraction step. *Id.* (describing the tandem affinity purification method as a useful tool to investigate protein complexes). The method therefore purifies a TAP-tagged protein. *See* page 1030, left column.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Gierde's method to isolate a protein from a protein pair by using NaCl to disrupt electrostatic interaction, as taught by Sukits. By combining Gierde and Sukits, Gierde's method would be modified to include a NaCl elution step on one of the immobilized protein-protein complexes described by Sukits. In this manner, the NaCl elution would separate one protein within the complex from other proteins. The skilled artisan would have made the modification because Sukit's technique allows the skilled artisan to purify and concentrate one of the proteins involved in NFκB activation to analyze this signaling pathway in an individual. Indeed, since Gierde indicates that analytes can be purified using affinity chromatography for various purposes, *see* paragraphs 0225-0226, including analyzing protein-protein interactions, the skilled artisan would recognize that analyzing a signaling pathway by isolating one of its constituents falls within Gierde's purpose. Moreover, since Gierde does not limit the elution to any particular method, the skilled artisan would have had a reasonable expectation of success in combining Sukits's technique with Gierde's affinity chromatography method.

One of ordinary skill in the art would have also found it obvious to modify Gierde's method by using a TAP-tagged protein. The skilled artisan would have made the modification because having two affinity tags allows for a second level of purification, which the skilled artisan would have recognized as producing a more purified eluant for analysis. Indeed, since Gierde teaches recombinant affinity-tagged proteins and multi-elution steps, *see* paragraph 0180, the skilled artisan would have

recognized the benefit of combining the two elements to allow for a more thorough purification technique.

II. Dependent claims 10-21 are obvious

Regarding claims 10-11, Rigaut teaches that TEV protease is used to cleave the TAP-tagged protein from the first affinity separation column. *See* Figure 1 and caption.

Regarding claim 12, Gierde describes that an extraction step which removes analyte from the affinity column can involve binding of the analyte to a specific cognate molecule. *See* paragraph 0143. One of ordinary skill would have found it obvious to use the same antibody coated on the affinity column as the specific cognate molecule. Indeed, because the coated antibody has known affinity for the analyte, the skilled artisan would have recognized that using the same antibody for the specific cognate molecule would produce the extraction sought.

Regarding claim 13, Gierde describes a method of performing step elutions, in which sequential elutions are performed using different types of gradients. *See* paragraphs 0181-0187. The gradients can be in any order and not required to be performed in a particular sequence. *See* paragraph 0185 (describing a first elution by increasing ionic strength and a second elution by affinity binding, but not limited to these specific elution gradients).

With respect to claims 14-15 and 20-21, the TAP tag comprises Staphylococcus Protein A that can bind to IgG. *See* Rigaut, page 1030, Figure 1 and caption. Regarding claims 20-21, it would have been obvious to one of ordinary skill in the art to use protein A as either the first or second affinity ligand - i.e., switch positions with

calmodulin binding peptide, since the purpose of Rigaut is simply to utilize dual-dimension affinity chromatography. Indeed, the genetic procedure to recombinantly produce the TAP tag could have placed protein A closer to the target protein.

With respect to claims 16-19, the TAP tag comprises calmodulin binding peptide, which can be separated from the protein via EGTA. *See* page 1030, left column, Figure 1 and caption. Moreover, TEV protease is used to cleave protein A from the calmodulin binding peptide. *Id.* Regarding claims 16-19, it would have been obvious to one of ordinary skill in the art to use the calmodulin binding peptide as either the first or second affinity ligand - i.e., switch positions with protein A, since the purpose of Rigaut is simply to utilize dual-dimension affinity chromatography. Indeed, the genetic procedure to recombinantly produce the TAP tag could have placed calmodulin binding peptide closer to the target protein.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gierde in view of Sukits as applied to claims 2 and 6 above, and further in view of Rigaut.

Gierde, described above, does not teach that the Protein A is derived from Staphylococcus aureus.

Rigaut, also described above, teaches Protein A from Staphylococcus aureus.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to apply Protein A from Staphylococcus aureus, as taught by Rigaut, to Gierde's method. The skilled artisan would have made the modification since Gierde already teaches Protein A and does not limit its source. Accordingly, since Rigaut's

Protein A is capable of acting as a tag in affinity chromatography, the skilled artisan would have found it obvious to substitute Rigaut's Protein A for Gierde's tag. For the same reason, the skilled artisan would have had a reasonable expectation of success.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gierde in view of Sukits as applied to claims 1 and 22-23 above, and further in view of U.S. Patent No. 5,007,934 to Stone and U.S. Patent No. 5,849,885 to Nuyens *et al*. ("Nuyens").

Gierde and Sukits, described above, do not teach a KCl chemical agent.

Stone describes using NaCl or KCl as equivalent salts for removing glycoprotein or proteoglycan associated with collagen through electrostatic interaction. *See* column 7, lines 60-66.

Nuyens describes NaCl or KCl as equivalent salts for reducing electrostatic interactions between lactoferrin and other proteins. *See* column 4, lines 51-60.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Gierde and Sukit's method to use KCl as the eluting compound instead of NaCl. The skilled artisan would have performed the modification because it is well known in the art to use KCl as a substitute for NaCl for disrupting electrostatic interactions between proteins, as evidenced by Stone and Nuyens. For the same reason, the skilled artisan would have had a reasonable expectation of success in substituting KCl for NaCl.

Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gierde in view of Sukits as applied to claims 1 and 34 above, and further in view of U.S. Patent Application Pub. 2003/0229212 to Fahrner *et al.* (“Fahrner”).

NaCl acts as a competitor for heparin, as evidenced by Gierde and Fahrner. Specifically, Gierde indicates that in ion-exchange chromatography, an analyte can be eluted by displacement using a salt. *See* paragraph 022. Fahrner describes an ion-exchange chromatography as a competition between an ion and a substrate for a molecule of interest. *See* paragraph 0008. Here, NaCl is used as an elution medium against two proteins in a multi-protein complex. *See supra* rejection of claim 1. In light of Gierde and Fahrner, the NaCl competes with the complex to elute a protein in the multi-protein complex, thereby binding to one of the proteins and meeting the claimed limitation.

Claims 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gierde in view of Sukits as applied to claim 1 above, and further in view of U.S. Patent 6,610,508 to Hentze *et al.* (“Hentze”) and evidenced by U.S. Patent No. 5,753,225 to Clary *et al.* ("Clary").

Gierde and Sukits do not teach the step of identifying protein-protein association as a putative cause for Alzheimer's disease.

Clary describes receptor-ligand complexes as reversible electrostatic attractions. *See* column 10, lines 66-67; column 11, lines 1-11.

Hentze describes a step of identifying protein-protein interactions in order to detect disease states, including Alzheimer's disease. *See* column 1, lines 33-54; column 30, lines 58-62.

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Gierde and Sukit’s method to include the step of identifying protein-protein interactions for detecting Alzheimer’s disease. The skilled artisan would have made the modification because detecting Alzheimer’s disease informs a patient whether the disease state is present. Moreover, the skilled artisan would have had a reasonable expectation of success because protein-protein interaction is a type of ligand-receptor interaction, which is known to be a reversible electrostatic attraction. *See* Clary, column 11, line 10. Hentze’s technique would therefore fit well with Gierde and Sukit’s method of utilizing electrostatic interactions.

Response to Arguments

Applicants traverse the rejection of the pending and active claims in the Response filed November 5, 2010. Applicants’ arguments, described below, are not convincing to overcome the prior art and allow the claims in their present form. However, since new grounds of rejection are presented (albeit using the same prior art references of record), this action is being made Non-Final.

Applicants first argue that the multi-protein complex described in the Gierde reference does not have support in the ‘595 priority document. *See* Response, pages

2-4. Notably, Applicants point to the Final Rejection, which cites to pages 72-73 of the 199-page document, and contend that this section does not provide the requisite support. *Id.* In a telephone interview conducted on October 7, 2010 (and followed by a telephone conversation on October 26, 2010), the Examiner agreed that the cited section in the '595 priority document does not provide support for a multi-protein complex. However, upon further review of the document, it is apparent that support lies elsewhere. For example, page 95 of the 199-page document describes a biotinylated antibody-antigen complex that is bound to an affinity column through biotin-streptavidin affinity tags. Accordingly, with this description, Gierde has written description support in the ‘595 priority document for a multi-protein complex bound to an affinity column.

Second, Applicants argue that the combination of Gierde, Sukits and Rigut is improper for a number of reasons. *See* pages 4-7. Specifically, Applicants contend that Rigaut allegedly does not teach or suggest that the second ligand must remain immobilized on the affinity column during elution of the first ligand. *See* page 4, last paragraph. However, Gierde teaches this limitation by describing multi-protein complexes in which one constituent of the complex is eluted while the other constituents remain on the affinity column. *See supra* rejection of claims 3 and 4. As noted above, this description has support in the priority document on page 95 of the 199-page document.

Applicants also opine that Sukits “never studied *in vivo* formed protein pairs” and that the *in vitro* experiments would not be viewed by the skilled artisan as having the

same results *in vivo*. *See* page 5, third paragraph. Although Sukits does not describe RIP DD-TRADD or TNFR-1-TRADD protein complexes *in vivo*, this would not deter the skilled artisan from considering Sukits's approach for *in vivo* formed pairs. Indeed, Applicants have not provided evidence that separation of *in vitro*-joined proteins necessarily require a different separation approach from *in vivo*-joined proteins. Accordingly, since Sukits provides evidence that NaCl can separate electrostatically-joined proteins, and that those proteins are found to be joined *in vivo*, the skilled artisan would have found it obvious to apply Sukits's technique to *in vivo*-joined protein pairs.

Along the same lines, Applicants argue that Sukits's description that the NaCl titration indicates that the protein-protein interaction is “at least in part electrostatic” suggests that other interactions may be present and confirms the notion that *in vitro* interaction does not relate to how the proteins come together *in vivo*. *See* page 5, third paragraph. However, even if other interactions are present, the fact that using NaCl alone can induce separation of joined proteins would be enough to induce the skilled artisan to consider using NaCl for *in vivo*-joined proteins. Indeed, some of those same "other interactions" may be present *in vitro*; however, these interactions did not have an affect upon the NaCl titration. Accordingly, the skilled artisan would not have been influenced by this portion of Sukits to forgo using NaCl to separate *in vivo*-joined proteins.

Applicants further argue that since Sukits teaches that increasing electrostatic forces leads to dissociation of noncovalently-joined proteins, the skilled artisan would expect that the second ligand described by Gierde would also be eluted since it is

noncovalently bound to the affinity matrix. *See* page 6, second and third paragraphs. Accordingly, Applicants opine that the skilled artisan would not have combined the cited references since there is allegedly no expectation that the second ligand would remain immobilized as claimed. However, Gierde and Rigaut describe the same affinity tags that are claimed in the instant application. Indeed, dependent claims 7, 9, 15, 17, 19 and 21 recite, amongst other tags, GST, CBP, MBP and Staphylococcus aureus Protein A. Gierde describes the GST, CBP and MBP tags. *See* paragraph 0092. Rigaut describes the Protein A tag. *See* Figure 1 and caption. Accordingly, since GST, CBP, MBP and Protein A keep the second ligand immobilized as claimed, and Gierde and Rigaut teach the same tags, the combination of Gierde and Sukits (as applied to independent claims 1 and 2 and their dependents) and the combination of Gierde, Sukits and Rigaut (as applied to independent claims 3 and 4 and their dependents) would necessarily allow elution of the first ligand by applying NaCl while keeping the second ligand immobilized on the affinity column.

For the foregoing reasons, Applicants' arguments are not convincing to overcome the cited prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Nelson Yang/
Primary Examiner, Art Unit 1641